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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/670,907	09/25/2003	Gisele Veilleux	GOUD:037US/10311165	6020

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EXAMINER	
HOLT, ANDRIAE M	

ART UNIT	PAPER NUMBER
1616	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/670,907	VEILLEUX ET AL.	
	Examiner	Art Unit	
	Andriae M. Holt	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 July 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,6-9 and 11-28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-2, 6-9, and 11-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The Examiner of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Examiner Andriae M. Holt.

This Office Action is in response to Applicant's amendments filed July 2, 2008. Claims 1-2, 6-9, and 11-28 are pending in the application. Claims 1-2 and 11-12 have been amended. Claims 13-28 are newly added. Claims 1-2, 6-9, and 11-28 will presently be examined to the extent they read on the elected subject matter of record.

Status of the Claims

Rejections not reiterated from the previous Office Action are hereby withdrawn. The following rejections are either reiterated or newly applied. They constitute the complete set of rejections and/or objections presently being applied to the instant application.

Claim Objections

Applicant is advised that should claims 1, 2, 25, and 26 be found allowable, claims 23, 24, 27, and 28 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-2, 6-9, and 11-28 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant has "new matter" recited in the claims. Applicant claims in step a) of claims 1, 2, 23, and 24 different "shapes". Applicant has support in the specification for different granular sizes, but does not provide any disclosure that the powders additionally have different "shapes".

Applicant also claims "wherein the method does not comprise addition of a loss-compensatory overage amount of Pyridoxine HCl". Applicant discloses on page 2, first paragraph, that when processing both active ingredients through the same equipment, more pyridoxine HCl is lost than doxylamine succinate. Applicant discloses that to compensate for the lose of pyridoxine HCl; operators have commonly used an 8-10 weight percent overage of pyridoxine HCl in comparison to doxylamine succinate. Applicant also discloses on page 10, first paragraph, the results demonstrate that by using the manufacturing method of the present invention, the average loss of pyridoxine HCl was dramatically lowered when compared to the prior art method. Applicant does not specifically state that the method "does not comprise addition of a loss-

compensatory overage amount of pyridoxine HCl". It states that it was discovered that the average loss was lowered, not that an overage was not needed or used.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-2, 6-9, and 11-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chen (US Pat. 5,260,069) in view of Chu et al. (US Pat. 6,419,954), Bishai et al., Gereg (US 2002/0039603), Dron (US 2002/0001652) and Crotts et al. (WO 02/092056).

Chen teaches a process of for preparation of pulsatile particles which can contain combinations of therapeutic agents in which the granule containing the active agents and swelling agent are prepared by the well known and economic roller compaction method with sieving to select granules of particular mesh size (Column 1, lines 56-68, Column 2, lines 60-65). It is taught that the particles can be contained in capsules or compressed into tablets with a binding agent which can dissolve promptly in any aqueous medium or be in the form of an enteric tablet to resist dissolution until after passing through the stomach (Column 5, lines 16-31).

Chu et al. teach embodiments in which a tablet can further include untreated active agents (e.g. without coating material or in powders) in addition to the active agent-containing particles and that the active agent particles can contain vitamins or drugs, such as in which the active agent can be vitamins or drugs, such as, doxylamine succinate (Column 9, lines 59-68, Column 10, lines 15, 16). It teaches that any suitable method for granulation can be used including roll compaction (Column 12, lines 25-44).

Bishai et al. teach that the combination of 10mg doxylamine succinate and 10 mg pyridoxine HCl is safe and effective in treating nausea and vomiting associated with pregnancy (NVP)(Pages 167, 170,173-177).

Gereg teaches that dry granulation is used when materials have sufficient inherent binding or cohesive properties to form granules. Gereg teaches dry granulation may also be performed using a "roller compactor." In a roller compactor material particles are consolidated and densified by passing the material between two high-pressure rollers. The densified material from a roller compactor is then reduced to a uniform granule size by milling. The uniform granules may then be mixed with other substances, such as a lubricant, to tablet the material (as, for example, by way of a rotary tableting machine) (similar sized granules, content uniformity). In addition to pharmaceutical use, roller compaction is used in other industries, such as the food industry, animal feed industry and fertilizer industry (pages 1-2 paragraph 14). Gereg teaches dry granulation has several advantages over wet granulation including its usefulness with respect to ingredients that are sensitive to moisture or unable to withstand elevated temperatures during drying, and because it does not use organic

solvents which may pose health and environmental hazards. There are also fewer steps involved in dry granulation than wet granulation. Dry granulation by means of roller compaction is an efficient and useful method of granulation capable of handling a large amount of material in a short period of time (dry granulation by "slugging," on the other hand, may be slow, inefficient, and many times requires several attempts at a successful formulation to ensure material flow) (page 2, paragraph 15).

Dron teaches roller compaction is a pressure agglomeration technique, well known and used in the pharmaceutical industry to provide materials with better content uniformity and handling properties (content uniformity). Dron teaches that typically, roller compaction is used in conjunction with an appropriate size reduction process (page 1, paragraph 8). Dron teaches in compaction granulation, typically a granulation process is utilized which first coarsely breaks the compacted material into larger than desired particles. These particles are then milled until they pass through a screen or perforated plate which has either a slightly larger or almost the same size opening as the upper limit of the desired particle size range. This material is then sieved using almost the same size opening as the lower limit of the desired particle size. The granules that remain on the sieve are collected as final product (page 1, paragraph 9).

Crotts et al. teach a roller compaction process to form consistent granules which upon encapsulation provide a substantially consistent dissolution profile among various lots of dosage formulation blends comprising the same bulk substance sodium phenytoin. Crotts et al. further teach the process also produces a reliable and consistent product of sodium phenytoin (page 5, lines 25-29). Crotts et al. teach the process

comprises the steps of adding sodium phenytoin to a vessel or bowl of a blender and adding at least one excipient to the vessel. Crotts et al. teach the resultant blend is transferred to a roller compactor and compacted between at least two rollers to form a compact with the excipient. Crotts et al. further teach the pressure imparted on the blend enhances the physical adhesion between the sodium phenytoin and the excipient. Crotts et al. teach the compact is subsequently milled to form a granulation. The resultant granulation is then formed into the desired dosage form, such as capsules (page 6, lines 3-11). Crotts et al. teach the roller compactor functions by uniformly applying pressure on a mixed powder blend by passing the blend between two counter-rotating rollers. Crotts et al. teach the pressure imparted on the blend by the rollers compresses the powder into a compact, such as a sheet or ribbon, which is typically milled to produce granules (content uniformity) (page 7, lines 25-28). Crotts et al. teach the process relates to the discovery that some therapeutic agents can be formulated and processed to yield a dosage form providing sustained blood plasma concentration of the active pharmaceutical ingredient (page 7, lines 29-30-page 8, lines 1-2).

The difference between the prior art and the claimed invention is that the prior art does not expressly disclose the use of more than one active ingredient, such as the combination of doxylamine succinate and pyridoxine HCl. The prior art amply suggests the combination of doxylamine succinate and pyridoxine HCl as the prior art teaches that the granules can include combinations of therapeutic agents, such as vitamins and doxylamine succinate. Bishai et al. teach the combination of doxylamine succinate and pyridoxine HCl and that pyridoxine HCL and doxylamine succinate are provided in

different granular sizes. The prior art amply discloses preparation of granules containing active ingredients and excipients by the well known method of roller compaction and sieving to obtain appropriate mesh size granules which are used for form pulsatile particles which are compressed into enteric coated tablets or enclosed in capsules. The prior art teaches, Gereg, Dron, and Crotts et al., the roller compaction method provides uniform and consistent dosage formulations. Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated to try the roller compaction method to provide uniform and consistent dosage formulation of doxylamine succinate and pyridoxine because all of the prior art cited teaches that roller compaction is the best dry granulation method to use to formulate uniform and consistent dosage formulations.

The prior art is silent as to the method not comprising the addition of loss-compensatory overage amounts of Pyridoxine HCl. However, since the prior art teaches that processes using compaction rollers in which the size of the particles can be selected form uniform and consistent formulations, it would have been well within the skill of one of ordinary skill in the art to select a particle size which was sufficiently large enough to avoid loss during processing. The size of the particles is a well known factor in the loss of the active ingredient due to adherence to processing equipment and the use of more processing equipment. In addition, the repeated steps in a given processing equipment increase the opportunities of loss due to adherence. As such, one of ordinary skill in the art would not expect the pyridoxine HCl particles to adhere to

the roller in any significant amount as upon compaction the pyridoxine HCl will no longer consist of individual small particles, which would mean less loss of the active ingredient.

Therefore, the claimed invention, as a whole, would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, because every element of the invention has been collectively taught by the combined teachings of the references.

Response to Declaration

The declaration under 37 CFR 1.132 filed July 2, 2008, is insufficient to overcome the rejection of claims 1-2, 6-9, and 11-28 based upon 35 U.S.C. 103(a) as set forth in the Office action because of the following reasons: 1) lack of comparison to the closest prior art, 2) no true side-by-side comparison, 3) lack of data provided in the declaration. The Declaration does not provide a comparison of the closest cited prior art. The Declaration provides information into the thought process of the inventors and the steps taken to decide to use roller compaction as the method for preparing the pharmaceutical dosage forms. The Declaration does not provide side by side comparison dosage forms prepared using Applicant's invention and dosage forms using the prior art method. Thus, no results were presented in the declaration to show unexpected or unobvious data. There is a comparison presented in the Specification on pages 7-11, examples, 1 and 2. However, the results are not unexpected based on the prior art teachings that in a roller compactor material particles are consolidated and densified by passing the material between two high-pressure rollers. The densified

material from the roller compactor is then reduced to a uniform granule size by milling. The uniform granules may then be mixed with other substances (Gereg, US 2002/0039603, page 1, paragraph 14). As such, one of ordinary skill in the art would not expect the pyridoxine HCl particles to adhere to the roller in any significant amount as upon compaction the pyridoxine HCl will no longer consist of individual small particles.

Therefore, based on the cited reasons, the Declaration is insufficient and the claims remain rejected.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Andriae M. Holt whose telephone number is (571)272-9328. The examiner can normally be reached on 7:00 am-4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Richter Johann can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Andriae M. Holt
Patent Examiner
Art Unit 1616

/John Pak/
Primary Examiner, Art Unit 1616